Supplemental Material

DDT and Malaria Prevention: Addressing the Paradox

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Mini overview – DDT studies on human health effects published in 2009

Since the Pine River Statement, more studies on human health effects have been published; some also from developing countries. We conducted a PubMed search for studies published in 2009 using the same search terms as the Pine River Statement (Eskenazi et al. 2009); (DDT OR DDE) AND (toxicity OR health OR cancer OR carcinogenicity OR reproduction OR estrogen OR neurological OR development OR exposure OR diabetes OR pregnancy OR miscarriage OR spontaneous abortion OR birth weight OR gestation OR lactation OR birth defects OR growth OR puberty OR fertility OR neurotoxicity OR neurodevelopment OR immunological). We found 22 epidemiological papers relating to human health effects. A short overview of each, relevant to the main paper, is included below. For more details, the individual papers should be consulted.

- Rignell-Hydbom et al. (2009a) and Turyk et al. (2009) reported strong associations between *p,p'*-DDE and type 2 diabetes in two prospective studies on two very different populations (371 women from southern Sweden, and 503 sport fish consumers from the Great Lakes, USA, respectively.
- Self-reported diabetes was associated with *p,p'*-DDE and some PCB congener levels in serum from a First Nation community in Canada (101 participants, odds ratio 6.1; 95% confidence interval 1.37-27.30) (Philibert et al. 2009).

- Lopez-Espinoza et al. (2009) found that pregnant Spanish mothers (1st trimester) with higher levels of p,p'-DDE had significantly higher thyroid-stimulating hormone (TSH) and lower free thyroxine in blood (n = 157).
- p,p'-DDE and some PCBs were significantly higher in young Akwasasne Mohawk adults (10-17 years) with high anti-thyroid peroxidase antibodies (n = 61 males and 57 females; Schell et al. 2009).
- DDE was not implicated in associations between organochlorine levels and free thyroxine (FT4) in serum of 38 New York State anglers (Bloom et al. 2009b).
- Bloom et al. (2009a) found significant changes in levels of organochlorine compounds in the serum of women (prospective study of 79 participants) from pre-conception to birth covering critical development windows, and suggest that sampling efforts should coincide with specific development windows.
- A case control study (158 Italian women from Rome) found significantly higher serum levels of *p,p'*-DDE (p = 0.01) and most of the PCBs in women with endometriosis (Porpora et al. 2009). However, no significant increase of endometriosis was associated with *p,p'*-DDE.
- Pan et al. (2009) found no consistent association between DDT and DDE in breast milk and infant development, but did report a significant association between *p,p'*-DDE and 12-month old boys scoring below average on the Mullen Scales of Early Learning (n = 231) and the Short Form: Level I (infant) on the MacArthur-Bates Communicative Development Inventories for 8-18 month olds (n = 218). DDE in milk however, was associated with scoring below average on the gross motor scale in males in the first 12 months (OR = 1.9; 95% confidence interval 1.1 – 3.3) but not in females (OR = 0.7; 95% confidence intervals 0.3 – 1.5, with likelihood ratio test p = 0.02); the first time this difference has been reported. This study was conducted in North Carolina, USA
- Impaired neurodevelopment may however, be reversed or does not persist after 12 months of age of children prenatally exposed to DDE, in the state of Morelos, Mexico (Torres-Sánchez et al. 2009).
- Verhulst et al. (2009) found that intrauterine exposure to DDE and PCBs was significantly associated with increased Body Mass Index during early childhood in 138 randomly chosen mother-infant pairs from Flanders, Belgium. The association with DDE was significant in 3 year old children, and smoking seemed to enhance this effect.
- Among a number of associations, significant positive associations of *p,p'*-DDT and *p,p'*-DDD, but not *p,p'*-DDE in cord blood, were found with baby length, birth weight, and head circumference in a group of 41 cesarean section babies born in Singapore (Tan et al. 2009).

- Increased serum *p,p'*-DDE levels in 259 mothers from a Michigan were significantly associated with increased birth weight (regression coefficient 9.22, $p < 0.05$) and body mass index (regression coefficient 2.88, $p < 0.05$; both for p,p'-DDE levels in serum > 2.9 µg/l) suggesting that maternal exposure to DDE during pregnancy is linked to overweight in adult female offspring (Karmaus et al. 2009).
- Serum folate was significantly negatively associated with serum *p,p'*-DDT and *p,p'*-DDE, and serum cysteine was negatively associated with serum *p,p'*-DDT, *p,p'*-DDD and *p,p'*-DDE in a study of 296 non-smoking female textile workers in China (Arguelles et al. 2009).
- Rignell-Hydbom et al. (2009b) found a weak positive association between *p,p'*-DDE and bone mineral density of 911 postmenopausal women (between 60 - 70 years old) in Sweden. It is therefore unlikely that *p,p'*-DDE is a risk factor for osteoporosis at the detected concentrations (maximum 18 ng/l)
- Ward et al. (2009) found no association between DDE and DDT with childhood leukemia in California (184 leukemia cases, and 212 case matched controls).
- Purdue et al. (2009) found, with a nested case control study in Norway, an association between *p,p'*-DDE (and other OCs) in serum and testicular germ cell tumors, although the association was not significant ($p = 0.07$ for p,p'-DDE, 49 cases, with 51 case matched controls).
- Itoh et al. (2009), in a matched case-control study, found no association between serum organochlorine concentrations (that included *p,p'*-DDE, *p,p'*-DDT, and *o,p'*-DDT) and breast cancer in 403 Japanese case matched pairs of women.
- Porta et al. (2009), in a cross-sectional study in Spain, found that patients with pancreatic ductal adrenocarcinoma (PDA) whose tumors had a *KRAS* mutation (n = 81), had significantly higher serum levels of *p,p*'-DDT and PCB-138 and PCB-153 (all $p < 0.05$) than patients admitted for only benign, non-digestive, disorders (n = 22). Only PCB-138 had a dose-response pattern. An association with coffee intake was also found, and independent roles in aetiopathogenisis of PDA were suggested.
- No organochlorine pesticides (including DDE) had any associations with serum testosterone levels in adult Native American men (n = 257) or women (n = 436), but PCBs did in the male group (Goncharov et al. 2009).
- Messaros et al. (2009) reported significant associations between *p,p'*-DDE serum levels and reduced sperm concentration, motility, and morphology (depending on DNA polymorphs) in 336 Michigan (USA) men presenting at infertility clinics. Unadjusted for DNA morphology (all cases), the risk for low sperm concentration was significantly

increased (OR = 2.53; 95% confidence interval 1.0 - 6.31) by high DDE and DDT in serum.

- De Jager et al. (2009) found that increased *p,p'*-DDE in serum was associated with a moderate but significant (p = 0.031) increase in chromatin defects in sperm of 209 young men from DDT-sprayed dwellings in South Africa.
- Although published in 2010, this study needs mentioning due to its malaria reference. Bornman et al. (2010) reported a study on 3 310 baby boys from South Africa in a DDT-sprayed area, and found a significantly increased probability that boys from DDT-sprayed homes would have urogenital birth defects (odds ratio 1.33, 95% confidence interval 1.04–1.72). Being a homemaker (term equivalent to stay-at-home mother or full-time caregiver) more exposed to IRS DDT instead of being employed outside the home further significantly increased the risk of having a baby with an urogenital defect by 41% (odds ratio 1.41, 95% confidence interval 1.13–1.77).

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